**REMARKS**

The Office Action has been carefully reviewed. No claim is allowed. Non-elected claims 1, 2, 5-16 and 20 are cancelled without prejudice to filing a divisional application thereon. Claims 3, 4, 17-19 and 21 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claims 3, 4 and 17-18 have been objected to as being of improper dependent form. Appropriate correction is made, thereby obviating this objection.

The drawings, specifically Figures 1, 10 and 12, have been objected to because the clarity and resolution of Figures 1, 10 and 12 fail to show the banding patterns as described in the specification. Replacement sheets for Figures 1, 10 and 12 are attached for review and approval by the examiner.

Claims 3, 4 and 17-19 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

Part of this rejection with respect to the terms "alteration" and "an expression regulatory sequence" is obviated by the amendment to the claims.

Regarding the term "GILR", this acronym stands for Glucocorticoid Induced Leucine-Zipper family Related gene (GILR),

as supported at paragraph [0029] of the specification. In the same paragraph [0029], it is also disclosed that the term Glucocorticoid Induced Leucine-Zipper gene (GILZ) can be used synonymously. As the term GILZ is now much more commonly used in the art, the claims are amended to recite Glucocorticoid Induced Leucine Zipper gene (GILZ) in place of GILR, thereby obviating this rejection.

Claims 3, 4 and 17-19 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement for any genus of transgenic mice that are defined solely by the increased expression of any GILR RNA or protein in its T cell lineage. This rejection is respectfully traversed.

The written description of "mammalian T-cell lineage specific promoter" can be found, for example on page 63, lines 17-19 of the specification, where it is disclosed that "the nucleotide sequence encoding a protein of interest is operably linked to a mammalian T-cell lineage-specific promoter to generate recombinant construct or "transgene" that is then introduced into the fertilized embryo". The specification further discloses a representative number of known mammalian T-cell lineage specific promoter in the paragraph [00215] bridging pages 63 and 64. Thus, applicant has described a list

of selected promoters that are known to be T-cell lineage-specific promoters. Moreover, the sequences of these promoters are known as well as the procedures to isolate and operably linked them to the recited cDNA. Example 2 in the specification discloses a specific example of the presently claimed transgenic mice in detail. The mammalian T-cell lineage specific promoter used in that example is the human CD2 promoter.

With due respect to the examiner, applicant emphasizes that the "written description" requirement must be applied in the context of the claimed invention and the state of the knowledge in the art. The presently claimed invention is not directed to discovering which promoters are related to a T-cell lineage, for that is in the prior art, but in the production of novel transgenic mice having in their genome a novel nucleic acid construct to achieve novel results. A person of skill in the relevant art of the present invention would know that these known promoters would retain their activity to express GILR (GILZ) in a T-cell lineage specific manner.

Concerning the written description of "a mammalian GILR cDNA sequence", a general disclosure of the GILR cDNA sequences can be found, for example, on page 12 paragraphs [0029] of the specification. More specific description of two mammalian GILR cDNA sequences, the mouse and human sequences (see paragraphs

[0029] and [0030] and SEQ ID NOs: 1 and 5). Example 2 of the specification also provides a specific example of the presently claimed transgenic mice in detail, where the mammalian GILR cDNA sequence T used in the example is the mouse GILR cDNA.

The disclosure in the specification that is needed to meet the written description requirement varies with the nature and scope of the invention at issue, and with the scientific and technical knowledge already in existence. Applicant submits that adequate description and exemplification of the present invention has been provided in the specification as would be understood by those of skill in the relevant art. U.S. case law illustrates that the determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the maturity of the science or technology (see, e.g., In re Wallach, 378 F.3d 1330, 1333-34 (Fed. Cir. 2004)). In the present application, the production of transgenic mice was a mature technology at the time of the priority filing date and the specification presents not only general teachings of how to select the nucleic acid construct comprising a mammalian T-cell lineage specific promoter operably linked to a mammalian GILR cDNA sequence, and to produce transgenic mice expressing GILR in their T-cell lineage at an elevated level compared to non-transgenic mice, but also specific examples of the production

of such claimed transgenic mice. Accordingly, the genus of transgenic mice presently claimed is fully described by the species exemplified.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 3, 4 and 17-19 have been rejected under 35 U.S.C. §112, first paragraph, because the examiner states that the specification does not reasonably provide enablement for a transgenic mouse with any nucleic acid construct comprising any GILR cDNA from any species operably linked to any mammalian T-cell lineage specific expression regulatory sequence, wherein said mouse expresses GILR in its T cell lineage at an elevated level compared to a non-transgenic mouse and wherein the expression of GILR results in any alteration of the thymocyte subset composition and caspase-3 activation, a method of using any such transgenic mouse for screening compounds having glucocorticoid-related effects, or a method of making any such transgenic mouse. The specification is however considered enabling for a transgenic mouse with a nucleic acid construct comprising an 874 bp mouse GILR cDNA operably linked to a human CD2 promoter and a human CD2 locus control region integrated into its genome, wherein said mouse expresses the GILR protein in its T-cell lineage at an elevated level, compared to a non-transgenic

mouse, wherein the elevated level of GILR protein expression results in a significant decrease in $CD4^+$ $CD8^+$ double positive, and increases in $CD4^-$ $CD8^-$ double negative, $CD8^+$ single positive cells and $CD4^+$ subpopulation, compared with a non-transgenic mouse, and increased caspase 3 activation, to a method for producing the transgenic mouse, and to using the transgenic mouse in a screening method. This rejection is respectfully traversed.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include, for example, the amount of direction provided by the specification and the existence of working examples. In view of these criteria, applicant submits that the present invention is fully enabled to one of skill in the art. The specification discloses on page 63, lines 17-19 the "mammalian T-cell lineage specific promoter" that can be used in the present invention. More specific disclosure of known mammalian T-cell lineage specific promoters is further provided in the paragraph [00215] bridging pages 63 and 64. A list of selected promoters that are known to be T-cell lineage-specific promoters is disclosed as discussed above in the written description rejection. Moreover, the sequences of these

promoters are known as well as the procedures to isolate them and operably linked them to the claimed cDNA. Applicant refers to Example 2 of the specification where a specific example of the presently claimed mice is disclosed in detail. The mammalian T-cell lineage specific promoter used in the example is the human CD2 promoter.

The specification also discloses mammalian GILR cDNA sequences. A general description of the GILR cDNA sequences can be found for example on page 12, paragraph [0029] of the specification. The applicant also points to more specific description of two mammalian GILR cDNA sequences: the mouse and human sequences (see paragraphs [0029] and [0030] and SEQ ID NOs: 1 and 5). Example 2 of the specification, a specific example of the presently claimed transgenic mice is disclosed in detail. The mammalian GILR cDNA sequence used in the example is the mouse GILR cDNA. Based on homology to mouse GILR, the human homolog was isolated. Accordingly, other homologs from mammalian species can be readily isolated using one or both of the mouse and human GILR sequences.

Accordingly, in view of the amendment to the claims to limit the scope of the expression regulatory sequence to a promoter, the GILR cDNA to a mammalian GILR (GILZ) cDNA sequence (of which the human and mouse sequences are exemplified), and the

level of GILR expressed in the transgenic mouse to be elevated compared to a non-transgenic mouse, and of the guidance provided in the specification, one of skill in the art would be fully enabled for the scope claimed in the presently amended set of claims.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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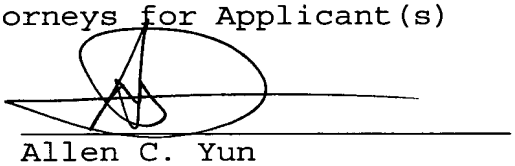
By 
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**Amendments to the Drawings:**

Figures 1, 10 and 12 are indicated as failing to show the banding patterns as described in the specification because of poor resolution and clarity. The attached replacement sheets including Figs. 1, 10 and 12, replace the original sheets of drawings, Figs. 1, 10 and 12.

Attachments: Replacement Sheets